132502 Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Jeffrey Rayes Examiner #: 78264 Date: 9/14/04
Art Unit: 1625 Phone Number 30 272-0691 Serial Number: 10/614,266
Mail Box and Bldg/Room Location: Rem 470C / Rem 4A68 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): Lee Bibb Copy

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search the enclosed
Process Thanks
Jeff

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STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: Noble	NA Sequence (#) _____	STN 399
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Date Searcher Picked Up: _____	Bibliographic ✓	Dr.Link _____
Date Completed: 9/17/04	Litigation _____	Lexis/Nexis _____
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Online Time: 46	Other _____	Other (specify) _____

PTO-1590 (8-01)

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     FILE 'HCAPLUS' ENTERED AT 14:27:08 ON 17 SEP 2004
L1            1 US20040152782/PN

     FILE 'REGISTRY' ENTERED AT 14:27:22 ON 17 SEP 2004

     FILE 'HCAPLUS' ENTERED AT 14:27:24 ON 17 SEP 2004
L2              TRA L1 1- RN :       36 TERMS

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L3           36 SEA L2

     FILE 'WPIX' ENTERED AT 14:27:27 ON 17 SEP 2004
L4            1 US20040152782/PN

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FILE LAST UPDATED: 16 Sep 2004  (20040916/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

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L1   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:80637  HCAPLUS
DN   140:151932
ED   Entered STN:  01 Feb 2004
TI   Preparation of polymorphic forms of nateglinide
IN   Yahalomi, Ronit; Shapior, Evgeny; Dolitzky, Ben-zion; Gozlan, Yigael;
     Gome, Boaz
PA   Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical Usa, Inc.
SO   PCT Int. Appl., 130 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  C07C231-24
     ICS  C07C233-63; A61K031-16; A61P003-00
CC   63-6 (Pharmaceuticals)
     Section cross-reference(s): 75
FAN.CNT 3
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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PI   WO 2004009532        A1    20040129    WO 2003-US22375        20030718
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
             NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
             GW, ML, MR, NE, SN, TD, TG
     US 2004152782         A1    20040805    US 2003-614266         20030703 <--
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US 2004116526	A1	20040617	US 2003-623237	20030718
WO 2004067496	A1	20040812	WO 2004-US839	20040113

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PRAI	US 2002-396904P	P	20020718
	US 2002-413622P	P	20020925
	US 2002-414199P	P	20020926
	US 2002-423750P	P	20021105
	US 2002-432093P	P	20021210
	US 2002-432962P	P	20021212
	US 2003-442109P	P	20030123
	US 2003-449791P	P	20030224
	US 2003-479016P	P	20030616
	US 2003-614266	A	20030703
	US 2002-393495P	P	20020703
	US 2003-622905	A2	20030718
	WO 2003-US22375	A2	20030718
	US 2003-693166	A2	20031023
	US 2003-746697	A2	20031224

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004009532	ICM	C07C231-24
	ICS	C07C233-63; A61K031-16; A61P003-00

AB The invention discloses the preparation of 26 characterized forms of nateglinide (forms A, C, D, F, G, I, J, K, L, M, N, O, P, Q, T, U, V, Y, .alpha., .beta., .gamma., .delta., .epsilon., .sigma., .theta. and .OMEGA.). Most of the forms are solvates (with the exception of forms L, P, U, .alpha., .delta. and .sigma.). Polymorphic forms are characterized by their mp, DSC, XRPD, FTIR; form interconversion is also discussed. For example, D-phenylalanine is reacted with trans-[[4-(isopropyl)cyclohexanee]carbonyl]chloride (i. NaOHaq; ii. H2SO4). The wet cake of nateglinide is dissolved in EtOAc, the aqueous phase is removed and the resulting solution heated to 50.degree. under reduced pressure and added to hot heptane. The resulting solution is cooled and seeded with the B-form to afford the .delta.-form (33% yield).

ST polymorphic nateglinide blood sugar lowering prepn

IT Fluidized beds
(dryers; preparation of polymorphic forms of nateglinide)

IT Drying apparatus
(fluidized-bed; preparation of polymorphic forms of nateglinide)

IT Solvents
(nateglinide solvate; preparation of polymorphic forms of nateglinide)

IT Crystal nucleation
Crystallization
Human
Polymorphism (crystal)
Slurries
(preparation of polymorphic forms of nateglinide)

IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood, lowering, treatment; preparation of polymorphic forms of nateglinide)

IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 71-23-8, n-Propanol, uses 71-36-3, n-Butanol, uses 75-05-8, Acetonitrile, uses 75-52-5, Nitromethane, uses 78-93-3, Methyl ethyl ketone, uses 108-10-1, Methyl isobutyl ketone 108-88-3, Toluene, uses 110-54-3, Hexane, uses 141-78-6, Ethyl acetate, uses 142-82-5, Heptane, uses 563-80-4, Methyl isopropyl ketone 1330-20-7, Xylene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(nateglinide solvate; preparation of polymorphic forms of nateglinide)

IT 67-66-3, Chloroform, uses 109-99-9, Tetrahydrofuran, uses 123-91-1, Dioxane, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of polymorphic forms of nateglinide)

IT 105816-04-4P, Nateglinide
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)

(preparation of polymorphic forms of nateglinide)
IT 105816-04-4DP, Nateglinide, polymorphs 651353-42-3P 651353-43-4P
651353-44-5P 651353-45-6P 651353-46-7P 651353-47-8P 651353-48-9P
651353-49-0P 651353-50-3P 651353-51-4P 651353-52-5P 651353-53-6P
651353-54-7P
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of polymorphic forms of nateglinide)
IT 673-06-3, D-Phenylalanine 84855-54-9, trans-[[4-(Isopropyl)cyclohexane]carbonyl]chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of polymorphic forms of nateglinide)
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Ajinomoto Co Inc; EP 1334963 A 2003 HCAPLUS
(2) Ajinomoto Co Inc; EP 1334964 A 2003 HCAPLUS
(3) Alembic Ltd; WO 03022251 A 2003 HCAPLUS
(4) Koguchi, Y; US 5463116 A 1995 HCAPLUS
(5) Koguchi, Y; WO 2003087039 2003 HCAPLUS
(6) Kumashiro, I; US 4816484 A 1989 HCAPLUS
(7) LI, G; YAOWU FENXI ZAZHI 2001, V21(5), P342 HCAPLUS
(8) Sumikawa, M; WO 2002034713 A 2002 HCAPLUS
(9) Takahashi, D; WO 2002032854 A 2002 HCAPLUS

=> b wpix
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FILE LAST UPDATED: 15 SEP 2004 <20040915/UP>
MOST RECENT DERWENT UPDATE: 200459 <200459/DW>
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=> d all l4

L4 ANSWER 1 OF 1 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-180282 [17] WPIX
CR 2004-108803 [11]; 2004-594140 [57]
DNC C2004-071244
TI New crystalline polymorphic forms of nateglinide useful for lowering the blood sugar level.
DC B05
IN DOLITZKY, B; GOME, B; GOZLAN, Y; SHAPIOR, E; YAHALOMI, R; SHAPIRO, E
PA (TEVA-N) TEVA PHARM IND LTD; (DOLI-I) DOLITZKY B; (GOME-I) GOME B; (GOZL-I) GOZLAN Y; (SHAP-I) SHAPIRO E; (YAHA-I) YAHALOMI R; (TEVA-N) TEVA PHARM USA INC
CYC 105
PI WO 2004009532 A1 20040129 (200417)* EN 130 C07C231-24
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
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US 2004116526 A1 20040617 (200440) A61K031-198

AU 2003253971 A1 20040209 (200450) C07C231-24
US 2004152782 A1 20040805 (200452) A61K031-198 <--

ADT WO 2004009532 A1 WO 2003-US22375 20030718; US 2004116526 A1 Provisional US 2002-396904P 20020718, Provisional US 2002-413622P 20020925, Provisional US 2002-414199P 20020926, Provisional US 2002-423750P 20021105, Provisional US 2002-432093P 20021210, Provisional US 2002-432962P 20021212, Provisional US 2003-442109P 20030123, Provisional US 2003-449791P 20030224, Provisional US 2003-479016P 20030616, US 2003-623237 20030718; AU 2003253971 A1 AU 2003-253971 20030718; US 2004152782 A1 Provisional US 2002-393495P 20020703, Provisional US 2002-396904P 20020718, Provisional US 2002-413622P 20020925, Provisional US 2002-414199P 20020926, Provisional US 2002-423750P 20021105, Provisional US 2002-432093P 20021210, Provisional US 2002-432962P 20021212, Provisional US 2003-442109P 20030123, Provisional US 2003-449791P 20030224, US 2003-614266 20030703

FDT AU 2003253971 A1 Based on WO 2004009532

PRAI US 2003-614266 20030703; US 2002-396904P 20020718;
US 2002-413622P 20020925; US 2002-414199P 20020926;
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US 2002-432962P 20021212; US 2003-442109P 20030123;
US 2003-449791P 20030224; US 2003-479016P 20030616;
US 2003-623237 20030718; US 2002-393495P 20020703

IC ICM A61K031-198; C07C231-24
ICS A61K031-16; A61P003-00; C07C231-02; C07C233-63

AB WO2004009532 A UPAB: 20040907
NOVELTY - 26 Crystalline nateglinide forms as characterized by XRPD patterns, DSC thermograms and FTIR spectra, fully described in the specification, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the preparation of the crystalline forms of nateglinide.

ACTIVITY - Antidiabetic.

No test details for antidiabetic activity are given.

MECHANISM OF ACTION - None given.

USE - The pharmaceutical formulation comprising crystalline nateglinide form of A, C, D, F, G, I, J, K, M, N O, Q, T, V, Y, gamma, epsilon, theta or omega is useful to lower the blood sugar level (claimed).

ADVANTAGE - The new polymorphic forms of nateglinide provides a new opportunity to improve the performance characteristics of a pharmaceutical product.

Dwg.0/64

FS CPI

FA AB; DCN

MC CPI: B10-C04A; B14-S06

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STRUCTURE FILE UPDATES:   15 SEP 2004  HIGHEST RN 745743-57-1
DICTIONARY FILE UPDATES:  15 SEP 2004  HIGHEST RN 745743-57-1

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http://www.cas.org/ONLINE/DBSS/registryss.html

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L10  ANSWER 1 OF 3  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   62067-45-2  REGISTRY
CN   Cyclohexanecarboxylic acid, 4-(1-methylethyl)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Cyclohexanecarboxylic acid, 4-isopropyl- (6CI, 7CI)
OTHER NAMES:
CN   4-Isopropylcyclohexanecarboxylic acid
CN   NSC 28951
FS   3D CONCORD
MF   C10 H18 O2
LC   STN Files:   BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CSCHEM,
       PS, RTECS*, SPECINFO, TOXCENTER, USPATFULL
         (*File contains numerically searchable property data)
DT.CA  CAplus document type:  Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); PREP (Preparation); RACT
       (Reactant or reagent); USES (Uses); NORL (No role in record)
RL.NP  Roles from non-patents:  PREP (Preparation); RACT (Reactant or reagent);
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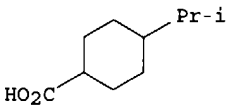


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

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             13 REFERENCES IN FILE CAPLUS (1907 TO DATE)
              4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L10  ANSWER 2 OF 3  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   7084-93-7  REGISTRY
CN   Cyclohexanecarboxylic acid, 4-(1-methylethyl)-, cis- (9CI)  (CA INDEX
     NAME)
OTHER CA INDEX NAMES:
CN   Cyclohexanecarboxylic acid, 4-isopropyl-, cis- (8CI)
OTHER NAMES:
CN   cis-4-Isopropylcyclohexanecarboxylic acid
CN   cis-p-Menthan-7-oic acid
FS   STEREOSEARCH
MF   C10 H18 O2
LC   STN Files:   BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMLIST, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**, NDSL**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA  CAplus document type:  Conference; Journal; Patent
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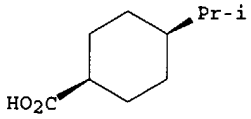
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); NORL (No role in record)

Relative stereochemistry.



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1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L10 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
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CN Cyclohexanecarboxylic acid, 4-isopropyl-, trans- (8CI)
OTHER NAMES:
CN trans-4-Isopropylcyclohexanecarboxylic acid
CN trans-p-Menthan-7-oic acid
FS STEREOSEARCH
MF C10 H18 O2
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, PS, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
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DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
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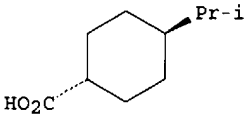
Relative stereochemistry.



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1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **84855-54-9** REGISTRY
CN Cyclohexanecarbonyl chloride, 4-(1-methylethyl)-, trans- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN trans-[[4-(Isopropyl)cyclohexane]carbonyl]chloride
FS STEREOSEARCH
MF C10 H17 Cl O
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, PS, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent

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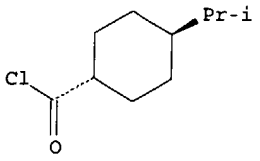
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Relative stereochemistry.



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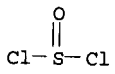
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

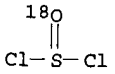
=> => d ide l16 tot

L16 ANSWER 1 OF 10 REGISTRY COPYRIGHT 2004 ACS on STN
RN 176913-21-6 REGISTRY
CN **Thionyl chloride, radical ion(1+) (9CI)** (CA INDEX NAME)
MF **Cl2 O S**
CI RIS
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation); PRP (Properties); RACT (Reactant or reagent)



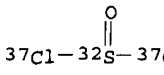
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L16 ANSWER 2 OF 10 REGISTRY COPYRIGHT 2004 ACS on STN
RN 101410-89-3 REGISTRY
CN **Thionyl-18O chloride (9CI)** (CA INDEX NAME)
MF **Cl2 O S**
SR CA
LC STN Files: CA, CAPLUS, CASREACT
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)



7 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L16 ANSWER 3 OF 10 REGISTRY COPYRIGHT 2004 ACS on STN
RN 87897-65-2 REGISTRY
CN **Thionyl-32S chloride-37Cl2 (9CI)** (CA INDEX NAME)
MF **Cl2 O S**
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PRP (Properties)



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L16 ANSWER 4 OF 10 REGISTRY COPYRIGHT 2004 ACS on STN
RN 87897-64-1 REGISTRY
CN **Thionyl-32S chloride-35Cl-37Cl (9CI)** (CA INDEX NAME)
MF **Cl2 O S**
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
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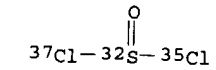

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L16 ANSWER 5 OF 10 REGISTRY COPYRIGHT 2004 ACS on STN
RN 87897-63-0 REGISTRY
CN **Thionyl-32S chloride-35Cl2 (9CI)** (CA INDEX NAME)
MF **Cl2 O S**
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
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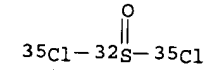
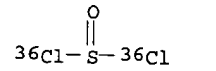


2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L16 ANSWER 6 OF 10 REGISTRY COPYRIGHT 2004 ACS on STN
RN 55207-92-6 REGISTRY
CN **Thionyl chloride-36Cl2 (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN **Thionyl chloride-36Cl**
MF **Cl2 O S**
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)



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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L16 ANSWER 7 OF 10 REGISTRY COPYRIGHT 2004 ACS on STN
RN 38323-75-0 REGISTRY
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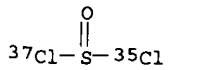
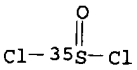
MF **Cl2 O S**
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PRP (Properties)



3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L16 ANSWER 8 OF 10 REGISTRY COPYRIGHT 2004 ACS on STN
RN 31602-28-5 REGISTRY
CN **Thionyl-35S chloride (8CI)** (CA INDEX NAME)
MF **Cl2 O S**

LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation)



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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L16 ANSWER 9 OF 10 REGISTRY COPYRIGHT 2004 ACS on STN
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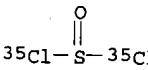
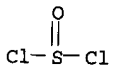
CN **Thionyl chloride-35Cl2 (8CI, 9CI)** (CA INDEX NAME)
MF **Cl2 O S**
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PRP (Properties)



3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L16 ANSWER 10 OF 10 REGISTRY COPYRIGHT 2004 ACS on STN
RN 7719-09-7 REGISTRY
CN **Thionyl chloride (8CI, 9CI)** (CA INDEX NAME)
OTHER NAMES:
CN Sulfinyl chloride
CN Sulfinyl dichloride
CN Sulfur chloride oxide (Cl2SO)
CN Sulfur chloride oxide (SCl2O)
CN Sulfur oxychloride
CN Sulfur oxychloride (SOCl2)
CN Sulfurous dichloride
CN Sulfurous oxychloride
CN **Thionyl chloride (SOCl2)**
CN **Thionyl dichloride**
FS 3D CONCORD
MF **Cl2 O S**
CI COM
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DETHERM*, DIPPR*, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Preprint; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5679 REFERENCES IN FILE CA (1907 TO DATE)
114 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5689 REFERENCES IN FILE CAPLUS (1907 TO DATE)
19 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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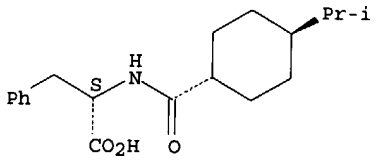
L42 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 105816-05-5 REGISTRY
CN L-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Phenylalanine, N-[[4-(1-methylethyl)cyclohexyl]carbonyl]-, trans-
OTHER NAMES:
CN **L-Nateglinide**
FS STEREOSEARCH
MF **C19 H27 N O3**
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)

Absolute stereochemistry.



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8 REFERENCES IN FILE CA (1907 TO DATE)
8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L42 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 105816-04-4 REGISTRY
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN D-Phenylalanine, N-[[4-(1-methylethyl)cyclohexyl]carbonyl]-, trans-
OTHER NAMES:
CN (-)-N-[(trans-4-Isopropylcyclohexyl)carbonyl]-D-phenylalanine
CN A 4166
CN AY 4166
CN **D-Nateglinide**
CN DJN 608
CN Fastic
CN **Nateglinide**
CN SDZ-DJN 608
CN Senaglinide
CN Starlix
CN Starlix DS
CN Starsis
FS STEREOSEARCH
DR 418766-62-8
MF **C19 H27 N O3**
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO,

CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

DT.CA CAplus document type: Journal; Patent

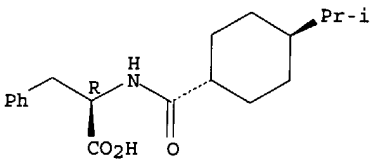
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
301 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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FILE 'REGISTRY' ENTERED AT 14:27:22 ON 17 SEP 2004

FILE 'HCAPLUS' ENTERED AT 14:27:24 ON 17 SEP 2004
L2 TRA L1 1- RN : 36 TERMS

FILE 'REGISTRY' ENTERED AT 14:27:24 ON 17 SEP 2004
L3 36 SEA L2

FILE 'WPIX' ENTERED AT 14:27:27 ON 17 SEP 2004
L4 1 US20040152782/PN

FILE 'REGISTRY' ENTERED AT 14:38:28 ON 17 SEP 2004
L5 7102 C10H18O2
L6 1534 L5 AND C6/ES
L7 1021 L6 NOT ((PMS OR IDS OR MAN)/CI OR UNSPECIFIED OR COMPD OR COMPO
L8 97 L7 AND CARBOXYLIC ACID
L9 7 L8 AND ISOPROPYL
SEL RN 2 4 5
L10 3 E1-3
L11 453 C10H17CLO
L12 4 L11 AND C6/ES AND ISOPROPYL
SEL RN 1
L13 1 E4
L14 101 CL2OS
L15 99 L14 AND THIONYL
L16 10 L15 NOT ((PMS OR IDS OR MAN OR MXS)/CI OR COMPOUND OR COMPD OR

FILE 'HCAPLUS' ENTERED AT 14:52:19 ON 17 SEP 2004
L17 72 L9
L18 5 (ISOPROPYLCYCLOHEXANECARBOXYLIC OR CYCLOHEXANECARBOXYLIC) (1A)
L19 7 L13
L20 1 ISOPROPYL (1A) CYCLOHEXANE (1A) CARBONYL (1A) CHLORIDE
L21 21176 L16 OR (SULFINYL OR SULPHINYL OR THIONYL) (1A) (CHLORIDE OR DIC
L22 26 L17-18 (L) RACT+NT/RL

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L23        11096 L21 (L) RACT +NT/RL
L24            3 L19-20 (L) PREP+NT/RL
L25            6 L19-20 (L) RACT+NT/RL
L26            0 L22 AND L23
L27            4 L17-18 AND L21
L28            1 L27 AND L19-20
                 E YAHALOMI R/AU
L29            2 E4
                 E SHAPIRO E/AU
L30          167 E3-4,E50-53
                 E DOLITZKY B/AU
L31           34 E4
                 E GOZLAN Y/AU
L32            4 E3,E5
L33            1 L27 AND L29-32
L34            1 L28 AND L29-32
L35            3 L17-18 AND L19-20
L36            1 L35 AND L29-32
L37            2 L35 NOT L36
L38            3 L27 NOT L34

     FILE 'REGISTRY' ENTERED AT 15:08:38 ON 17 SEP 2004
                 E NATEGLINIDE/CN
L39            1 E3
L40         1532 C19H27NO3
L41         1483 L40 NOT ((PMS OR IDS OR MAN)/CI OR COMPD OR COMPOUND OR UNSPECI
L42            2 L41 AND NATEGLINIDE

     FILE 'HCAPLUS' ENTERED AT 15:10:31 ON 17 SEP 2004
L43          300 L42
L44          257 PHENYLALANINE (3A)METHYLETHYL(1A) CYCLOHEXYL (1A) CARBONYL OR N
L45          682 A4166 OR AY4166 OR (A OR AY) (1A) 4166 OR 41 (1A) 66 OR DJN608
L46           19 L17-21 AND L43-45
L47            2 L46 AND L29-32
L48            2 L33 OR L34 OR L36 OR L47
L49           22 L37 OR L38 OR L46
L50           21 L49 AND (PY<=2002 OR AY<=2002 OR PRY<=2002 OR PD<20020703 OR AD

=> b hcap
FILE 'HCAPLUS' ENTERED AT 15:17:46 ON 17 SEP 2004
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FILE COVERS 1907 - 17 Sep 2004  VOL 141 ISS 13
FILE LAST UPDATED: 16 Sep 2004  (20040916/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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L48  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:80637  HCAPLUS
DN   140:151932
ED   Entered STN:  01 Feb 2004
TI   Preparation of polymorphic forms of nateglinide
IN   Yahalomi, Ronit; Shapior, Evgeny; Dolitzky, Ben-zion;
     Gozlan, Yigael; Gome, Boaz
PA   Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical Usa, Inc.
SO   PCT Int. Appl., 130 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
```

IC ICM C07C231-24
ICS C07C233-63; A61K031-16; A61P003-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 75
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004009532	A1	20040129	WO 2003-US22375	20030718
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004152782	A1	20040805	US 2003-614266	20030703
	US 2004116526	A1	20040617	US 2003-623237	20030718
	WO 2004067496	A1	20040812	WO 2004-US839	20040113
	W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
PRAI	US 2002-396904P	P	20020718		
	US 2002-413622P	P	20020925		
	US 2002-414199P	P	20020926		
	US 2002-423750P	P	20021105		
	US 2002-432093P	P	20021210		
	US 2002-432962P	P	20021212		
	US 2003-442109P	P	20030123		
	US 2003-449791P	P	20030224		
	US 2003-479016P	P	20030616		
	US 2003-614266	A	20030703		
	US 2002-393495P	P	20020703		
	US 2003-622905	A2	20030718		
	WO 2003-US22375	A2	20030718		
	US 2003-693166	A2	20031023		
	US 2003-746697	A2	20031224		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004009532	ICM	C07C231-24
	ICS	C07C233-63; A61K031-16; A61P003-00

AB The invention discloses the preparation of 26 characterized forms of **nateglinide** (forms A, C, D, F, G, I, J, K, L, M, N, O, P, Q, T, U, V, Y, .alpha., .beta., .gamma., .delta., .epsilon., .sigma., .theta. and .OMEGA.). Most of the forms are solvates (with the exception of forms L, P, U, .alpha., .delta. and .sigma.). Polymorphic forms are characterized by their mp, DSC, XRPD, FTIR; form interconversion is also discussed. For example, D-phenylalanine is reacted with trans-[[4-(isopropyl)cyclohexanee]carbonyl]chloride (i. NaOHaq; ii. H2SO4). The wet cake of **nateglinide** is dissolved in EtOAc, the aqueous phase is removed and the resulting solution heated to 50.degree. under reduced pressure and added to hot heptane. The resulting solution is cooled and seeded with the B-form to afford the .delta.-form (33% yield).

ST polymorphic **nateglinide** blood sugar lowering prepn

IT Fluidized beds
(dryers; preparation of polymorphic forms of **nateglinide**)

IT Drying apparatus
(fluidized-bed; preparation of polymorphic forms of **nateglinide**)

IT Solvents
(**nateglinide** solvate; preparation of polymorphic forms of **nateglinide**)

IT Crystal nucleation
Crystallization
Human
Polymorphism (crystal)
Slurries
(preparation of polymorphic forms of **nateglinide**)

IT 50-99-7, D-Glucose, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood, lowering, treatment; preparation of polymorphic forms of **nateglinide**)

IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 71-23-8, n-Propanol, uses 71-36-3, n-Butanol, uses 75-05-8, Acetonitrile, uses 75-52-5, Nitromethane, uses 78-93-3, Methyl ethyl ketone, uses 108-10-1, Methyl isobutyl ketone 108-88-3, Toluene, uses 110-54-3, Hexane, uses 141-78-6, Ethyl acetate, uses 142-82-5, Heptane, uses 563-80-4, Methyl isopropyl ketone 1330-20-7, Xylene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(**nateglinide** solvate; preparation of polymorphic forms of **nateglinide**)

IT 67-66-3, Chloroform, uses 109-99-9, Tetrahydrofuran, uses 123-91-1, Dioxane, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of polymorphic forms of **nateglinide**)

IT **105816-04-4P**, **Nateglinide**
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(preparation of polymorphic forms of **nateglinide**)

IT **105816-04-4DP**, **Nateglinide**, polymorphs 651353-42-3P 651353-43-4P 651353-44-5P 651353-45-6P 651353-46-7P 651353-47-8P 651353-48-9P 651353-49-0P 651353-50-3P 651353-51-4P 651353-52-5P 651353-53-6P 651353-54-7P
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of polymorphic forms of **nateglinide**)

IT 673-06-3, D-Phenylalanine **84855-54-9**, trans-[[4-(**Isopropyl**)**cyclohexane**]**carbonyl**]**chloride**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of polymorphic forms of **nateglinide**)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Ajinomoto Co Inc; EP 1334963 A 2003 HCAPLUS
(2) Ajinomoto Co Inc; EP 1334964 A 2003 HCAPLUS
(3) Alembic Ltd; WO 03022251 A 2003 HCAPLUS
(4) Koguchi, Y; US 5463116 A 1995 HCAPLUS
(5) Koguchi, Y; WO 2003087039 2003 HCAPLUS
(6) Kumashiro, I; US 4816484 A 1989 HCAPLUS
(7) LI, G; YAOWU FENXI ZAZHI 2001, V21(5), P342 HCAPLUS
(8) Sumikawa, M; WO 2002034713 A 2002 HCAPLUS
(9) Takahashi, D; WO 2002032854 A 2002 HCAPLUS

L48 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:41431 HCAPLUS
DN 140:94292
ED Entered STN: 18 Jan 2004
TI Process for preparing **nateglinide** and its intermediates
IN **Yahalomi, Ronit**; **Shapiro, Evgeny**; **Dolitzky, Ben-zion**; **Gozlan, Yigael**
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C231-02
ICS C07C231-24; C07C233-63; C07C051-60; C07C061-08
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004005240	A1	20040115	WO 2003-US21238	20030703
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2004116526	A1	20040617	US 2003-623237	20030718
PRAI	US 2002-393495P	P	20020703		
	US 2002-396904P	P	20020718		
	US 2002-413622P	P	20020925		
	US 2002-414199P	P	20020926		
	US 2002-423750P	P	20021105		
	US 2002-432093P	P	20021210		
	US 2002-432962P	P	20021212		
	US 2003-442109P	P	20030123		
	US 2003-449791P	P	20030224		
	US 2003-479016P	P	20030616		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004005240	ICM	C07C231-02
	ICS	C07C231-24; C07C233-63; C07C051-60; C07C061-08

OS CASREACT 140:94292

AB A process for the preparation of **nateglinide** involves converting trans-4-isopropylcyclohexanecarboxylic acid into the acid chloride by reaction with **thionyl chloride** in the presence of an organic amide and acylation of a suitable salt of D-phenylalanine with the acid chloride in a single or two phase system or in water free of a co-solvent.

ST **nateglinide** prepn; isopropylcyclohexanecarboxylic acid chloride prepn acylation phenylalanine

IT **105816-04-4P**, **Nateglinide**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of **nateglinide**)

IT 673-06-3, D Phenylalanine **7077-05-6**, trans-4 Isopropylcyclohexanecarboxylic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of **nateglinide**)

IT **84855-54-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of **nateglinide**)

IT 173653-89-9
RL: PRP (Properties)
(properties of **nateglinide** hydrate)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Ajinomoto Kk; EP 1334963 A 2003 HCAPLUS
(2) Koguchi, Y; US 5463116 A 1995 HCAPLUS
(3) Kumashiro, I; US 4816484 A 1989 HCAPLUS
(4) Shinkai, H; JOURNAL OF MEDICINAL CHEMISTRY 1989, V32(7), P1436 HCAPLUS
(5) Takahashi, D; WO 2002032854 A 2002 HCAPLUS
(6) Zhu, X; HECHENG HUAXUE 2001, V9(6), P537 HCAPLUS

=> d all l50 tot

L50 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:182826 HCAPLUS
DN 140:199745
ED Entered STN: 05 Mar 2004
TI Synthesis and purification of **nateglinide**
IN Naik, Samir Jaivant; Kulkarni, Pramila Vijay; Gaikwad, Nandkumar Baburao; Sawant, Mangesh Shivram; Bhirud, Shekhar; Batchu, Chandrasekhar
PA Glenmark Pharmaceuticals Limited, India
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C231-14
ICS C07C233-63
CC 34-2 (Amino Acids, Peptides, and Proteins)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004018408	A1	20040304	WO 2003-IB3270	20030812 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

Searched by Noble Jarrell

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG
PRAI IN 2002-MU777 A 20020826 <--
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004018408	ICM	C07C231-14
	ICS	C07C233-63

OS MARPAT 140:199745
AB N-[(trans-4-**isopropylcyclohexyl**)**carbonyl**]-D-**phenylalanine** (**nateglinide**) was prepared by reaction of trans-4-isopropylcyclohexylcarboxylic acid with an alkyl chloroformate in a ketonic solvent in the presence of a base at -20 to 30.degree.C and reaction of the mixed anhydride product with an aqueous alkali salt solution of D-phenylalanine. An example shows the synthesis of **nateglinide** by using triethylamine and Et chloroformate in acetone (97% pure following HPLC).
ST **nateglinide** prepn purifn; phenylalanine isopropylcyclohexylcarbonyl prepn purifn
IT **105816-04-4P**, **Nateglinide**
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(synthesis and purification of **nateglinide**)
IT 79-22-1, Methyl chloroformate 108-23-6, Isopropyl chloroformate 109-61-5, Propyl chloroformate 541-41-3, Ethyl chloroformate 673-06-3, D Phenylalanine **7077-05-6**, trans 4 Isopropylcyclohexanecarboxylic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and purification of **nateglinide**)
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Ajinomoto Kk; JP 07017899 A 1995 HCAPLUS

L50 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:80637 HCAPLUS
DN 140:151932
ED Entered STN: 01 Feb 2004
TI Preparation of polymorphic forms of **nateglinide**
IN Yahalomi, Ronit; Shapior, Evgeny; Dolitzky, Ben-zion; Gozlan, Yigael; Gome, Boaz
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical Usa, Inc.
SO PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C231-24
ICS C07C233-63; A61K031-16; A61P003-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 75
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004009532	A1	20040129	WO 2003-US22375	20030718 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004152782	A1	20040805	US 2003-614266	20030703 <--
	US 2004116526	A1	20040617	US 2003-623237	20030718 <--
	WO 2004067496	A1	20040812	WO 2004-US839	20040113
	W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,				

BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,
LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,
MZ, MZ, NA, NI

PRAI	US 2002-396904P	P	20020718	<--
	US 2002-413622P	P	20020925	<--
	US 2002-414199P	P	20020926	<--
	US 2002-423750P	P	20021105	<--
	US 2002-432093P	P	20021210	<--
	US 2002-432962P	P	20021212	<--
	US 2003-442109P	P	20030123	
	US 2003-449791P	P	20030224	
	US 2003-479016P	P	20030616	
	US 2003-614266	A	20030703	
	US 2002-393495P	P	20020703	<--
	US 2003-622905	A2	20030718	
	WO 2003-US22375	A2	20030718	
	US 2003-693166	A2	20031023	
	US 2003-746697	A2	20031224	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004009532	ICM	C07C231-24
	ICS	C07C233-63; A61K031-16; A61P003-00

AB The invention discloses the preparation of 26 characterized forms of **nateglinide** (forms A, C, D, F, G, I, J, K, L, M, N, O, P, Q, T, U, V, Y, .alpha., .beta., .gamma., .delta., .epsilon., .sigma., .theta. and .OMEGA.). Most of the forms are solvates (with the exception of forms L, P, U, .alpha., .delta. and .sigma.). Polymorphic forms are characterized by their mp, DSC, XRPD, FTIR; form interconversion is also discussed. For example, D-phenylalanine is reacted with trans-[[4-(isopropyl)cyclohexanee]carbonyl]chloride (i. NaOHaq; ii. H2SO4). The wet cake of **nateglinide** is dissolved in EtOAc, the aqueous phase is removed and the resulting solution heated to 50.degree. under reduced pressure and added to hot heptane. The resulting solution is cooled and seeded with the B-form to afford the .delta.-form (33% yield).

ST polymorphic **nateglinide** blood sugar lowering prepn

IT Fluidized beds
(dryers; preparation of polymorphic forms of **nateglinide**)

IT Drying apparatus
(fluidized-bed; preparation of polymorphic forms of **nateglinide**)

IT Solvents
(**nateglinide** solvate; preparation of polymorphic forms of **nateglinide**)

IT Crystal nucleation
Crystallization
Human
Polymorphism (crystal)
Slurries
(preparation of polymorphic forms of **nateglinide**)

IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood, lowering, treatment; preparation of polymorphic forms of **nateglinide**)

IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 71-23-8, n-Propanol, uses 71-36-3, n-Butanol, uses 75-05-8, Acetonitrile, uses 75-52-5, Nitromethane, uses 78-93-3, Methyl ethyl ketone, uses 108-10-1, Methyl isobutyl ketone 108-88-3, Toluene, uses 110-54-3, Hexane, uses 141-78-6, Ethyl acetate, uses 142-82-5, Heptane, uses 563-80-4, Methyl isopropyl ketone 1330-20-7, Xylene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(**nateglinide** solvate; preparation of polymorphic forms of **nateglinide**)

IT 67-66-3, Chloroform, uses 109-99-9, Tetrahydrofuran, uses 123-91-1, Dioxane, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of polymorphic forms of **nateglinide**)

IT **105816-04-4P, Nateglinide**
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(preparation of polymorphic forms of **nateglinide**)

IT **105816-04-4DP**, **Nateglinide**, polymorphs 651353-42-3P
651353-43-4P 651353-44-5P 651353-45-6P 651353-46-7P 651353-47-8P
651353-48-9P 651353-49-0P 651353-50-3P 651353-51-4P 651353-52-5P
651353-53-6P 651353-54-7P
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of polymorphic forms of **nateglinide**)
IT 673-06-3, D-Phenylalanine **84855-54-9**, trans-[[4-(**Isopropyl**)**cyclohexane**]**carbonyl**]**chloride**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of polymorphic forms of **nateglinide**)
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Ajinomoto Co Inc; EP 1334963 A 2003 HCAPLUS
(2) Ajinomoto Co Inc; EP 1334964 A 2003 HCAPLUS
(3) Alembic Ltd; WO 03022251 A 2003 HCAPLUS
(4) Koguchi, Y; US 5463116 A 1995 HCAPLUS
(5) Koguchi, Y; WO 2003087039 2003 HCAPLUS
(6) Kumashiro, I; US 4816484 A 1989 HCAPLUS
(7) LI, G; YAOWU FENXI ZAZHI 2001, V21(5), P342 HCAPLUS
(8) Sumikawa, M; WO 2002034713 A 2002 HCAPLUS
(9) Takahashi, D; WO 2002032854 A 2002 HCAPLUS

L50 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:41431 HCAPLUS
DN 140:94292
ED Entered STN: 18 Jan 2004
TI Process for preparing **nateglinide** and its intermediates
IN Yahalomi, Ronit; Shapiro, Evgeny; Dolitzky, Ben-zion; Gozlan, Yigael
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C231-02
ICS C07C231-24; C07C233-63; C07C051-60; C07C061-08
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004005240	A1	20040115	WO 2003-US21238	20030703 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004116526	A1	20040617	US 2003-623237	20030718 <--
PRAI	US 2002-393495P	P	20020703	<--	
	US 2002-396904P	P	20020718	<--	
	US 2002-413622P	P	20020925	<--	
	US 2002-414199P	P	20020926	<--	
	US 2002-423750P	P	20021105	<--	
	US 2002-432093P	P	20021210	<--	
	US 2002-432962P	P	20021212	<--	
	US 2003-442109P	P	20030123		
	US 2003-449791P	P	20030224		
	US 2003-479016P	P	20030616		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004005240	ICM	C07C231-02
	ICS	C07C231-24; C07C233-63; C07C051-60; C07C061-08

OS CASREACT 140:94292
AB A process for the preparation of **nateglinide** involves converting trans-4-isopropylcyclohexanecarboxylic acid into the acid chloride by reaction with **thionyl chloride** in the presence of an

organic amide and acylation of a suitable salt of D-phenylalanine with the acid chloride in a single or two phase system or in water free of a co-solvent.

ST **nateglinide** prepn; isopropylcyclohexanecarboxylic acid chloride prepn acylation phenylalanine

IT **105816-04-4P**, **Nateglinide**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of **nateglinide**)

IT 673-06-3, D Phenylalanine **7077-05-6**, trans-4 Isopropylcyclohexanecarboxylic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of **nateglinide**)

IT **84855-54-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of **nateglinide**)

IT 173653-89-9
RL: PRP (Properties)
(properties of **nateglinide** hydrate)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Ajinomoto Kk; EP 1334963 A 2003 HCAPLUS
(2) Koguchi, Y; US 5463116 A 1995 HCAPLUS
(3) Kumashiro, I; US 4816484 A 1989 HCAPLUS
(4) Shinkai, H; JOURNAL OF MEDICINAL CHEMISTRY 1989, V32(7), P1436 HCAPLUS
(5) Takahashi, D; WO 2002032854 A 2002 HCAPLUS
(6) Zhu, X; HECHENG HUAXUE 2001, V9(6), P537 HCAPLUS

L50 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:892741 HCAPLUS
DN 139:369757
ED Entered STN: 14 Nov 2003
TI Process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (**nateglinide**)
IN Rajamahendra, Shanmughasamy; Aswathanarayanappa, Chandrashekar; Puthiaparampil, Tom Thomas; Sridharan, Madhavan; Ganesh, Sambasivam
PA Biocon India Limited, India
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C233-63
ICS A61K031-198
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 34, 75

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003093222	A1	20031113	WO 2002-IN114	20020429 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI WO 2002-IN114 20020429 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003093222	ICM	C07C233-63
	ICS	A61K031-198

AB Novel polymorph Form C of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (I; i.e., **nateglinide**) is produced having a different IR spectrum and X-ray diffraction patterns (presented) from previously known forms of I.

ST **nateglinide** prepn crystal polymorphism; isopropylcyclohexylcarbonylphenylalanine prepn crystal polymorphism

IT Drying
Filtration
(in a process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (

nateglinide))
IT Bases, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(in a process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (**nateglinide**))
IT Acids, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(inorg.; in a process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (**nateglinide**))
IT Diabetes mellitus
(non-insulin-dependent; process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (**nateglinide**) for the treatment of)
IT Antidiabetic agents
Polymorphism (crystal)
(process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (**nateglinide**))
IT Ligroine
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (**nateglinide**))
IT 1344-28-1, Alumina, uses
RL: NUU (Other use, unclassified); USES (Uses)
(base support; in a process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (**nateglinide**))
IT 110-86-1, Pyridine, reactions 121-44-8, Triethylamine, reactions 497-19-8, Sodium carbonate, reactions 584-08-7, Potassium carbonate 1310-58-3, Potassium hydroxide, reactions 1310-65-2, Lithium hydroxide 1310-73-2, Sodium hydroxide, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(base; in a process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (**nateglinide**))
IT **7077-05-6**, trans-4-Isopropylcyclohexanecarboxylic acid 13033-84-6, D-Phenylalanine methyl ester hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(in a process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (**nateglinide**))
IT 71760-04-8, Propanephosphonic acid anhydride
RL: RGT (Reagent); RACT (Reactant or reagent)
(mineral acid; in a process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (**nateglinide**))
IT **105816-04-4P**, **Nateglinide**
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); PREP (Preparation); PROC (Process)
(process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (**nateglinide**))
IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 75-09-2, Dichloromethane, uses 141-78-6, Ethyl acetate, uses 1300-21-6, Dichloroethane 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (**nateglinide**))
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Ajinomoto Co Inc; EP 196222 B1 1986
(2) Ajinomoto Co Inc; US 4816484 A 1986 HCAPLUS
(3) Li, G; Yaowu Fenxi Zazhi 2001, V21(5), P342 HCAPLUS
(4) Shinkai, H; Journal of Medicinal Chemistry 1989, V32(7), P1436 HCAPLUS
(5) Sumikawa; US 5463116 A 1995 HCAPLUS

L50 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:62632 HCAPLUS
DN 138:73015
ED Entered STN: 28 Jan 2003
TI Synthesis process for trans-4-isopropylcyclohexanecarboxylic acid

? RCO_2H not the halide

IN Gu, Lianquan; An, Linkun; Ma, Lin; Guo, Xindong; Huang, Zhishu
PA Zhongshan Univ., Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
IC ICM C07C061-08
ICS C07C051-36
CC 24-5 (Alicyclic Compounds)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1319583	A	20011031	CN 2001-107459	20010116 <--
PRAI CN 2001-107459		20010116 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
CN 1319583	ICM	C07C061-08
	ICS	C07C051-36

OS CASREACT 138:73015
AB The process comprises hydrogenating cumic acid in acetic acid in the presence of PtO2, recovering solvent, treating with 10-35% inorg. base (such as Ba(OH)2, Mg(OH)2, KOH, or NaOH) solution at 50-150.degree. for 10-20 h, neutralizing with HCl to pH 2, crystallizing, filtering, and recrystg. in methanol.
ST isopropylcyclohexanecarboxylic acid prepn
IT Isomerization
Isomerization catalysts
(synthesis of trans-4-isopropylcyclohexanecarboxylic acid via isomerization with base)
IT Bases, uses
RL: CAT (Catalyst use); USES (Uses)
(synthesis of trans-4-isopropylcyclohexanecarboxylic acid via isomerization with base)
IT 1309-42-8, Magnesium hydroxide 1310-58-3, Potassium hydroxide, uses 1310-73-2, Sodium hydroxide, uses 1314-15-4, Platinum dioxide 17194-00-2, Barium hydroxide
RL: CAT (Catalyst use); USES (Uses)
(synthesis of trans-4-isopropylcyclohexanecarboxylic acid as intermediate for **nateglinide**)
IT **105816-04-4P**, **Nateglinide**
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of trans-4-isopropylcyclohexanecarboxylic acid as intermediate for **nateglinide**)
IT 536-66-3, Cumic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of trans-4-isopropylcyclohexanecarboxylic acid as intermediate for **nateglinide**)
IT **62067-45-2P**, 4-Isopropylcyclohexanecarboxylic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of trans-4-isopropylcyclohexanecarboxylic acid as intermediate for **nateglinide**)
IT **7077-05-6P**, trans-4-Isopropylcyclohexanecarboxylic acid
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of trans-4-isopropylcyclohexanecarboxylic acid as intermediate for **nateglinide**)

L50 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:609152 HCAPLUS
DN 138:254901
ED Entered STN: 15 Aug 2002
TI a new synthesis method of **nateglinide** as antidiabetic drug
AU Wang, Dun; Liang, Yiheng; Gong, Ping; Zhao, Yanfang
CS School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SO Zhongguo Yaowu Huaxue Zazhi (**2002**), 12(2), 94-96
CODEN: ZYHZEF; ISSN: 1005-0108
PB Zhongguo Yaowu Huaxue Zazhi Bianjibu
DT Journal
LA Chinese
CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 63
OS CASREACT 138:254901
AB A new antidiabetic drug-**nateglinide** was synthesized from isopropylbenzene by Friedel-Crafts reaction, chloroform reaction,

catalytic hydrogenation to obtain trans-4-isopropylhexanecarboxylic acid, acylation of D-phenylalanine Et ester, hydrolysis to obtain **nateglinide** B-type crystal, and crystal-conversion. The total yield was 9.8%.

ST **nateglinide** antidiabetic drug synthesis

IT Antidiabetic agents
(of **nateglinide** and synthesis thereof)

IT Crystal structure types
(type B; of **nateglinide** as antidiabetic drug)

IT 63-91-2, L-Phenylalanine, reactions 75-36-5, Acetyl chloride 98-82-8, Isopropylbenzene 524-38-9 3081-24-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of **nateglinide** as antidiabetic drug)

IT 536-66-3P, 4-Isopropylbenzoic acid 645-13-6P, 4-Isopropylacetophenone **7077-05-6P**, trans-4-Isopropylcyclohexanecarboxylic acid 508170-82-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of **nateglinide** as antidiabetic drug)

IT **105816-04-4P**, **Nateglinide**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of **nateglinide** as antidiabetic drug)

L50 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:314896 HCAPLUS
DN 136:325825
ED Entered STN: 26 Apr 2002
TI Process for producing **nateglinide** crystals
IN Takahashi, Daisuke; Nishi, Seiichi; Takahashi, Satoji
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM C07C231-24
ICS C07C231-02; C07C233-63
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 75

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002032854	A1	20020425	WO 2001-JP9069	20011016 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001094265	A5	20020429	AU 2001-94265	20011016 <--
	EP 1334963	A1	20030813	EP 2001-974875	20011016 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001014729	A	20031014	BR 2001-14729	20011016 <--
	US 2004030182	A1	20040212	US 2003-418105	20030418 <--
PRAI	JP 2000-317604	A	20001018	<--	
	WO 2001-JP9069	W	20011016	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002032854	ICM	C07C231-24
	ICS	C07C231-02; C07C233-63

AB A process for producing **nateglinide** crystals comprises reacting trans-4-isopropylcyclohexylcarbonyl chloride with D-phenylalanine in a mixed solvent consisting of a ketone solvent and water in the presence of an alkali to obtain a reaction mixture containing **nateglinide**, adding an acid to the reaction mixture to make it acidic, and regulating (a) the temperature to 58.degree. to 72.degree. and (b) and the ketone solvent concentration to > 8 weight% and < 22 weight%, to conduct crystallization **Nateglinide** is a known antidiabetic. The process is an industrially advantageous method for crystallizing **nateglinide**.

ST **nateglinide** crystal prepn antidiabetic

IT Acylation

How the chloride was prep.?

(acylation of D-phenylalanine)
IT Crystal structure
(crystal structure of **nateglinide**)
IT Crystallization
(process for producing **nateglinide** crystals)
IT Alkali metal hydroxides
RL: RGT (Reagent); RACT (Reactant or reagent)
(process for producing **nateglinide** crystals)
IT Ketones, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvents; process for producing **nateglinide** crystals)
IT **105816-04-4P**, **Nateglinide**
RL: IMF (Industrial manufacture); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for producing **nateglinide** crystals)
IT 673-06-3, D-Phenylalanine **84855-54-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for producing **nateglinide** crystals)
IT 1310-58-3, Potassium hydroxide, reactions 7647-01-0, Hydrochloric acid, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(process for producing **nateglinide** crystals)
IT 67-64-1, Acetone, uses 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; process for producing **nateglinide** crystals)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Ajinomoto Co; EP 196222 A2 1986
(2) Ajinomoto Co; JP 6354321 A 1986
(3) Ajinomoto Co; JP 05208943 A 1993 HCAPLUS
(4) Ajinomoto Co; EP 526171 A2 1993 HCAPLUS

L50 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:314895 HCAPLUS
DN 136:340997
ED Entered STN: 26 Apr 2002
TI Process for preparation of acylphenylalanines
IN Sumikawa, Michito; Ohgane, Takao
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM C07C231-02
ICS C07C233-63
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002032853	A1	20020425	WO 2001-JP9068	20011016 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001094264	A5	20020429	AU 2001-94264	20011016 <--
	EP 1334962	A1	20030813	EP 2001-974874	20011016 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001014728	A	20031014	BR 2001-14728	20011016 <--
	TW 575541	B	20040211	TW 2001-90125695	20011017 <--
	US 2004024219	A1	20040205	US 2003-418102	20030418 <--
PRAI	JP 2000-317603	A	20001018	<--	
	WO 2001-JP9068	W	20011016	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002032853	ICM	C07C231-02
	ICS	C07C233-63

OS CASREACT 136:340997

AB This document discloses a process for preparing easily and simply high-purity acylphenylalanines extremely useful as raw materials of drugs or the like, characterized by reacting an acid chloride with phenylalanine in a mixed solvent consisting of an organic solvent and water under conditions made alkaline with potassium hydroxide.

ST acylphenylalanine prepn pharmaceutical raw material; acylation phenylalanine

IT Acylation
(Schotten-Baumann reaction of phenylalanine with acid chloride)

IT Acid halides
RL: RCT (Reactant); RACT (Reactant or reagent)
(acid chlorides; Schotten-Baumann reaction of phenylalanine with acid chloride)

IT 1310-58-3, Potassium hydroxide, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(Schotten-Baumann reaction of phenylalanine with acid chloride)

IT 2901-76-0P 36724-78-4P 56217-77-7P 56217-79-9P 56217-81-3P 74084-23-4P 103678-63-3P **105816-04-4P** 110882-63-8P 113535-11-8P 125572-71-6P 133849-18-0P 263706-10-1P 415964-23-7P 415964-24-8P 418766-67-3P 418766-68-4P 418766-69-5P 418766-70-8P 418766-71-9P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of acylphenylalanines)

IT 98-88-4, Benzoyl chloride 102-92-1, Cinnamoyl chloride 111-64-8, Caprylic acid chloride 112-13-0, Decanoic acid chloride 112-16-3, Lauric acid chloride 112-64-1, Myristic acid chloride 112-67-4, Palmitic acid chloride 112-76-5, Stearic acid chloride 112-77-6, Oleic acid chloride 142-61-0, Caproic acid chloride 673-06-3, D-Phenylalanine 874-60-2 1441-87-8, Salicyl chloride 2719-27-9, Cyclohexylcarbonyl chloride 10400-19-8, Nicotinoyl chloride 31093-30-8, Naphthoyl chloride **84855-54-9** 418766-63-9 418766-64-0 418766-65-1 418766-66-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of acylphenylalanines)

IT 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; Schotten-Baumann reaction of phenylalanine with acid chloride)

IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropyl alcohol, uses 67-64-1, Acetone, uses 75-05-8, Acetonitrile, uses 78-93-3, Methyl ethyl ketone, uses 109-99-9, THF, uses 123-91-1, Dioxane, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; process for preparation of acylphenylalanines)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Ajinomoto Co; JP 58189121 A 1983 HCAPLUS
(2) Ajinomoto Co; EP 93551 A2 1983 HCAPLUS
(3) Ajinomoto Co; EP 196222 A2 1986
(4) Ajinomoto Co; JP 6354321 A 1986
(5) Kao Corporation; JP 570418 A 1993
(6) Kao Corporation; JP 06157440 A 1994 HCAPLUS
(7) Kao Corporation; JP 06256276 A 1994 HCAPLUS

L50 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:174779 HCAPLUS

DN 137:370326

ED Entered STN: 11 Mar 2002

TI Synthesis of [14C]- and [3H]**DJN608 [STARLIX]**

AU Ray, T.; Ciszewska, G.; Wu, A.; Jones, L.

CS DMPK-Isotope Section, Novartis Pharmaceuticals, E. Hanover, NJ, USA

SO Synthesis and Applications of Isotopically Labelled Compounds, Proceedings of the International Symposium, 7th, Dresden, Germany, June 18-22, 2000 (**2001**), Meeting Date 2000, 228-231. Editor(s): Pleiss, Ulrich; Voges, Rolf. Publisher: John Wiley & Sons Ltd., Chichester, UK.
CODEN: 69CIJC; ISBN: 0-471-49501-8

DT Conference

LA English

CC 34-2 (Amino Acids, Peptides, and Proteins)

AB A novel oral medication for treating type 2 diabetes is trans-N-[[4-(1-**methylethyl**)**cyclohexyl**]-**carbonyl**]-D-**phenylalanine**, **DJN608 [Starlix]**. The key step in the synthesis of [14C]**DJN608** was the catalytic reduction of [carboxy-14C]cumic acid in the presence of PtO2 at 55 psi of hydrogen in acetic acid to give cis/trans-4-isopropylcyclohexane-[14C]carboxylic acid

in 3:1 ratio. Alternatively methods for preparing this mixture of cis- and trans- acids (3:1) are presented. Tritiated **DJN608** was prepared by reduction of the corresponding chloro derivative with tritium gas in the presence of 10% palladium on carbon.

ST isopropylcyclohexylcarbonylphenylalanine carbon 14 tritium labeled prepn; cumic acid carbon 14 prepn hydrogenation

IT Asymmetric synthesis and induction
(stereoselective preparation of [14C]- and [3H]**DJN608** [**Starlix**])

IT 536-66-3, 4-Isopropylbenzoic acid 586-61-8, 1-Bromo-4-isopropylbenzene 21685-51-8, D-Phenylalanine methyl ester 57292-44-1, N-tert.-Butoxycarbonyl-4-chloro-D-phenylalanine 109820-41-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereoselective preparation of [14C]- and [3H]**DJN608** [**Starlix**])

IT **7084-93-7P** 475168-18-4P 475168-20-8P 475168-24-2P, cis-1-Chloro-4-isopropylcyclohexane 475168-25-3P 475168-26-4P 475168-27-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation of [14C]- and [3H]**DJN608** [**Starlix**])

IT 475168-21-9P 475168-29-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of [14C]- and [3H]**DJN608** [**Starlix**])

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Barton, D; Tetrahedron Lett 1983, V24(45), P4979 HCAPLUS
(2) Sato, Y; Diabetes Res Clin Pract 1991, V12(1), P53 HCAPLUS
(3) Whitelaw, D; Diabetic Medicine 2000, V17(3), P225 HCAPLUS

L50 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:130037 HCAPLUS
DN 137:325603
ED Entered STN: 20 Feb 2002
TI Synthesis of **Nateglinide**
AU Zhu, Xue-yan; Peng, Ka; Wang, Xiao-qin; Yang, Li-ping
CS Dep. Chem., East China Normal Univ., Shanghai, 200062, Peop. Rep. China
SO Hecheng Huaxue (**2001**), 9(6), 537-540
CODEN: HEHUE2; ISSN: 1005-1511
PB Hecheng Huaxue Bianjibu
DT Journal
LA Chinese
CC 34-2 (Amino Acids, Peptides, and Proteins)
OS CASREACT 137:325603
AB Title compound, a new antidiabetes medicine, was synthesized from iso-propylbenzene in seven steps, giving the product with overall yield 22%.
ST **Nateglinide** synthesis isopropylbenzene antidiabetes drug
IT Diabetes mellitus
(non-insulin-dependent; of **Nateglinide**)
IT Antidiabetic agents
(of **Nateglinide**)
IT 7440-02-0, Raney nickel, uses
RL: CAT (Catalyst use); USES (Uses)
(catalysts; synthesis of **Nateglinide**)
IT **105816-04-4DP**, **Nateglinide**, B crystal type
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and crystalline forms of)
IT 98-82-8, Iso-propylbenzene 673-06-3, D-Phenylalanine 30525-89-4, Paraformaldehyde
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of **Nateglinide**)
IT 122-03-2P 536-66-3P 2051-18-5P **7077-05-6P** **62067-45-2P** **84855-54-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of **Nateglinide**)
IT **105816-04-4DP**, H crystal type
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of **Nateglinide**)

L50 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:38482 HCAPLUS

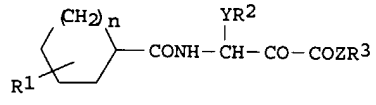
DN 134:100592
ED Entered STN: 16 Jan 2001
TI Preparation and effect of cycloalkylcarboxamide derivatives as cysteine protease inhibitors
IN Sato, Masaaki; Mukoyama, Harunobu; Kobayashi, Junichi; Tsuyuki, Shogo; Tokutake, Katsunori; Akabane, Satoshi
PA Kissei Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 27 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07C233-63
ICS A61K031-16; A61K031-195; A61K031-215; A61K031-44; A61K031-522; A61P043-00; C07C237-22; C07D213-56; C07D213-74; C07D473-08
CC 24-6 (Alicyclic Compounds)
Section cross-reference(s): 1, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2001011037	A2	20010116	JP 1999-188275	19990701 <--
PRAI JP 1999-188275		19990701 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 2001011037	ICM	C07C233-63
	ICS	A61K031-16; A61K031-195; A61K031-215; A61K031-44; A61K031-522; A61P043-00; C07C237-22; C07D213-56; C07D213-74; C07D473-08

OS MARPAT 134:100592
GI



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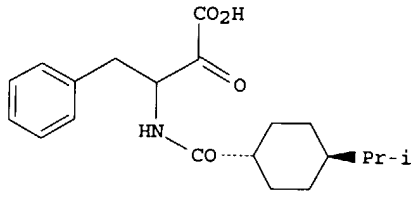


II

AB Title compds. [I; R1 = alkyl; Y = alkylene; R2 = OH, aryl, aryl alkoxy; R3 = H, alkyl, aryl, pyridyl, arylalkyl, pyridylalkyl; Z = O, NH; n = integer 1-3] and stereoisomers are prepared and possesses the cysteine protease inhibitory effect. Title compds. are useful in prevention of arthritis, Alzheimer's disease, rheumatism and osteoporosis. Thus, the title compound II was prepared and tested.
ST cycloalkylcarboxamide prepn cysteine protease inhibitor
IT Alzheimer's disease
Antiarthritics
Osteoporosis
Rheumatic diseases
(preparation and effect of cycloalkylcarboxamide derivs. as cysteine protease inhibitors)
IT 320358-08-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and effect of cycloalkylcarboxamide derivs. as cysteine

protease inhibitors)

IT 320358-11-0P 320358-14-3P 320358-16-5P 320358-20-1P 320358-22-3P 320358-24-5P 320358-26-7P 320358-28-9P 320358-32-5P 320358-34-7P 320358-36-9P, (RS)-3-(trans-4-Isopropylcyclohexylcarbonylamino)-2-oxo-4-phenyl-N-(3-phenylpropyl)butyric acid amide 320358-40-5P 320358-42-7P 320358-44-9P 320358-46-1P 320358-48-3P 320381-09-7P 320381-10-0P 320381-11-1P 320381-12-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and effect of cycloalkylcarboxamide derivs. as cysteine protease inhibitors)

IT 9001-92-7, Proteinase
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(preparation and effect of cycloalkylcarboxamide derivs. as cysteine protease inhibitors)

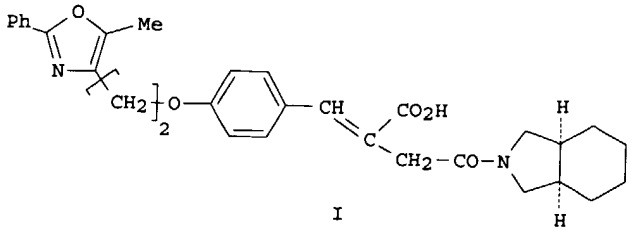
IT 100-46-9, Benzylamine, reactions 102-47-6, 1,2-Dichloro-4-chloromethylbenzene 1068-90-2 3978-80-1 **7077-05-6**, trans-4-Isopropylcyclohexanecarboxylic acid 16645-06-0, Dimethylhydroxylamine hydrochloride 24424-99-5, Di-tert-butyl dicarbonate 36935-19-0, D-Phenylalanine ethyl ester tosylate 38289-28-0 41038-69-1, 3-(3-Pyridyl)propylamine 56602-33-6, Benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate 87413-09-0 116661-86-0, (2S,3S)-3-tert-Butoxycarbonylamino-2-hydroxy-4-phenylbutyric acid 320357-95-7 320358-01-8 320381-06-4 320381-07-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and effect of cycloalkylcarboxamide derivs. as cysteine protease inhibitors)

IT 59331-63-4P **105816-04-4P** 114872-55-8P 185321-62-4P 320357-59-3P 320357-64-0P 320357-66-2P 320357-70-8P 320357-72-0P 320357-74-2P 320357-76-4P 320357-78-6P 320357-87-7P 320357-89-9P 320380-93-6P 320380-94-7P 320380-95-8P 320380-96-9P 320380-97-0P 320380-98-1P 320380-99-2P 320381-00-8P 320381-01-9P 320381-02-0P 320381-03-1P 320381-04-2P 320381-05-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and effect of cycloalkylcarboxamide derivs. as cysteine protease inhibitors)

IT 320357-99-1P 320358-03-0P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and effect of cycloalkylcarboxamide derivs. as cysteine protease inhibitors)

IT 320358-06-3P, Del all(RS)-3-(trans-4-n-Butylcyclohexylcarbonylamino)-4-(3,4-dichlorophenyl)-2-oxobutyric acid ethyl ester 320358-18-7P 320358-30-3P 320358-38-1P 320381-08-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and effect of cycloalkylcarboxamide derivs. as cysteine protease inhibitors)

L50 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:840649 HCAPLUS
DN 134:110109
ED Entered STN: 01 Dec 2000
TI Hybridization of non-sulfonylurea insulin secretagogue and thiazolidinedione-derived insulin sensitizer
AU Kitajima, Hiroshi; Nakamura, Mitsuharu; Tamakawa, Hiroki; Goto, Nobuharu
CS Department of Discovery Research, Welfide Corporation, Hirakata, 573-1153, Japan
SO Bioorganic & Medicinal Chemistry Letters (**2000**), 10(21), 2453-2456
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
CC 1-3 (Pharmacology)
Section cross-reference(s): 27, 28
GI



I

AB Hybrid compds. of non-sulfonylurea insulinotropic agents and thiazolidinedione-derived insulin-sensitizing agents were designed and synthesized. The benzylidenesuccinic acid derivative I was equal both to **nateglinide** in potency of insulin-releasing activity and to pioglitazone in insulin-sensitizing activity.

ST thiazolidinedione prepn insulinotropic insulin sensitizing structure

IT Antidiabetic agents
Structure-activity relationship
(preparation of thiazolidinediones as insulinotropics and insulin sensitizers)

IT Glycerides, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of thiazolidinediones as insulinotropics and insulin sensitizers)

IT 312688-50-9P 312688-51-0P 312688-52-1P 312688-78-1P 312688-83-8P
312688-84-9P 312688-85-0P 312688-87-2P 312688-89-4P 312688-91-8P
312688-92-9P 312688-99-6P 312689-16-0P 312689-17-1P 321371-24-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thiazolidinediones as insulinotropics and insulin sensitizers)

IT 9004-10-8, Insulin, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of thiazolidinediones as insulinotropics and insulin sensitizers)

IT 123-08-0, 4-Hydroxybenzaldehyde 123-25-1, Diethyl succinate 1470-99-1, cis-Hexahydroisoindoline 5223-06-3, 2-(5-Ethyl-2-pyridyl)ethanol **7077-05-6**, trans-4-Isopropylcyclohexanecarboxylic acid 18869-47-1, DL-Tyrosine methyl ester 50463-48-4 102029-44-7, (R)-4-Benzyl-1,3-oxazolidin-2-one 114393-97-4 144809-27-8 312689-77-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of thiazolidinediones as insulinotropics and insulin sensitizers)

IT 312689-54-6P 312689-55-7P 312689-57-9P 312689-59-1P 312689-73-9P
312689-80-8P 321371-23-7P 321371-25-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of thiazolidinediones as insulinotropics and insulin sensitizers)

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(6) Henke, R; J Med Chem 1998, V41, P5020
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(8) Ikenoue, T; Br J Pharmacol 1997, V120, P137 HCAPLUS
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(10) Kirk, J; J Fam Pract 1999, V48, P879 MEDLINE
(11) Kletzien, R; Mol Pharmacol 1991, V41, P393
(12) Lambert, D; Biochem Biophys Res Commun 1986, V140, P616 HCAPLUS
(13) Momose, Y; Chem Pharm Bull 1991, V39, P1440 HCAPLUS
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(15) Ohtani, K; J Endoclinol 1996, V150, P107 HCAPLUS
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(17) Shinkai, H; J Med Chem 1989, V32, P1436 HCAPLUS

(18) Shinkai, H; J Med Chem 1998, V41, P1927 HCAPLUS
(19) Sorbera, A; Drugs Future 1998, V23, P977

L50 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:468819 HCAPLUS
DN 123:55430
ED Entered STN: 06 Apr 1995
TI Preparation of trans-4-isopropylcyclohexanecarboxylic acid chloride
IN Matsuzawa, Toshihiro; Irie, Yasuo
PA Ajinomoto KK, Japan
SO Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07C061-15
ICS C07C051-60
CC 24-5 (Alicyclic Compounds)
FAN.CNT 1

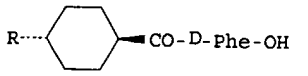
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 07017899	A2	19950120	JP 1993-163426	19930701 <--
PRAI JP 1993-163426		19930701 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 07017899	ICM	C07C061-15
	ICS	C07C051-60

OS CASREACT 123:55430
AB The title compound (I), useful as an intermediate for antidiabetic N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine, is prepared by treatment of trans-4-isopropylcyclohexanecarboxylic acid (II) with P chloride. II was treated with PCl5 in 1,2-dichloroethane at 40.degree. for 3 h to give 94% I and 0% the cis-isomer, whereas cis-isomer was detected, when SOCl2 was used instead of PCl5.
ST isopropylcyclohexanecarboxylic acid chloride prepn; chlorination phosphorus chloride isopropylcyclohexanecarboxylic acid
IT Antidiabetics and Hypoglycemics
Chlorination
(preparation of trans-4-isopropylcyclohexanecarboxylic acid chloride as intermediate for antidiabetic agent by chlorination of the acid with P chloride)
IT **105816-04-4P**
RL: PNU (Preparation, unclassified); PREP (Preparation)
(preparation of trans-4-isopropylcyclohexanecarboxylic acid chloride as intermediate for antidiabetic agent by chlorination of the acid with P chloride)
IT **7077-05-6**, trans-4-Isopropylcyclohexanecarboxylic acid
7719-12-2, Phosphorus trichloride 10026-13-8, Phosphorus pentachloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of trans-4-isopropylcyclohexanecarboxylic acid chloride as intermediate for antidiabetic agent by chlorination of the acid with P chloride)
IT **84855-54-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of trans-4-isopropylcyclohexanecarboxylic acid chloride as intermediate for antidiabetic agent by chlorination of the acid with P chloride)

L50 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:458305 HCAPLUS
DN 111:58305
ED Entered STN: 20 Aug 1989
TI N-(Cyclohexylcarbonyl)-D-phenylalanines and related compounds. A new class of oral hypoglycemic agents. 2
AU Shinkai, Hisashi; Nishikawa, Masahiko; Sato, Yusuke; Toi, Koji; Kumashiro, Izumi; Seto, Yoshiko; Fukuma, Mariko; Dan, Katsuaki; Toyoshima, Shigeshi
CS Cent. Res. Lab., Ajinomoto Co., Inc., Kawasaki, 210, Japan
SO Journal of Medicinal Chemistry (1989), 32(7), 1436-41
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
OS CASREACT 111:58305
GI



I

AB A series of analogs, e.g., I (R = alkyl, Ph), of N-(cyclohexylcarbonyl)-D-phenylalanine have been synthesized and evaluated for their hypoglycemic activity. Relationships were studied between the activity and the three-dimensional structure of the acyl moiety, which was characterized by high-resolution 1H NMR spectroscopy and MNDO calcns. The role of the carboxyl group of the phenylalanine moiety was also studied by comparing the activities of the enantiomers, the decarboxyl derivative, the esters, and the amides of the phenylalanine derivs. Thus, the structural requirements for possessing hypoglycemic activity was elucidated and a highly active compound, N-[(trans-4-**isopropylcyclohexyl**)**carbonyl**]-D-**phenylalanine** (I, R = CHMe2) was obtained, which showed a 20% blood glucose decrease at an oral dose of 1.6 mg/kg in fasted normal mice.

ST cyclohexylcarbonylphenylalanine prepn hypoglycemic; MNDO conformation cyclohexylcarbonylphenylalanine

IT Antidiabetics and Hypoglycemics
(cyclohexylcarbonylphenylalanine analogs as)

IT Conformation and Conformers
(of cyclohexylcarbonylphenylalanine analogs, by MNDO calcns.)

IT Molecular orbital
(MNDO, of cyclohexylcarbonylphenylalanine analogs, conformation in relation to)

IT Molecular structure-biological activity relationship
(hypoglycemic, of cyclohexylcarbonylphenylalanine analogs)

IT 98-73-7, 4-tert-Butylbenzoic acid 619-64-7, 4-Ethylbenzoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(catalytic hydrogenation of)

IT 536-66-3, 4-Isopropylbenzoic acid
RL: PRP (Properties)
(catalytic hydrogenation or peptide coupling of, with phenylalanine Me ester)

IT 64-04-0, 2-Phenylethylamine 47004-38-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with isopropylcyclohexanecarboxylic acid)

IT 17177-76-3P 75839-82-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and epimerization of)

IT 943-28-2P 6833-62-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and esterification of)

IT 85856-40-2P 105746-32-5P 105746-36-9P 105746-40-5P 105746-41-6P
105746-44-9P 105746-45-0P 105746-46-1P 105746-47-2P 105746-48-3P
105746-49-4P **105816-04-4P** 115732-16-6P 120927-36-8P
120927-37-9P 120927-38-0P 120927-39-1P 120927-40-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and hypoglycemic activity of)

IT 13828-36-9P 17177-75-2P 75839-91-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)

IT 943-29-3P, trans-4-tert-Butylcyclohexanecarboxylic acid 6833-47-2P
7084-93-7P, cis-4-Isopropylcyclohexanecarboxylic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and sequential peptide coupling of, with phenylalanine Me ester and saponification of)

IT **7077-05-6P**, trans-4-Isopropylcyclohexanecarboxylic acid
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and sequential peptide coupling reactions and saponification of)

IT 105746-37-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, amidation, hypoglycemic activity, and calculated conformation of)

IT 13828-35-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, epimerization, or saponification of)

IT 105746-38-1P 105746-39-2P 105816-06-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, hypoglycemic activity, and calculated conformation of)
IT 21685-51-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(sequential peptide coupling of, with carboxylic acids and saponification of)
IT 2577-90-4, Phenylalanine methyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(sequential peptide coupling of, with isopropylcyclohexanecarboxylic acid and saponification of)
IT 98-89-5, Cyclohexanecarboxylic acid 824-62-4, Bicyclo[2.2.1]heptane-2-carboxylic acid 1460-16-8, Cycloheptanecarboxylic acid 1466-73-5, trans-4-Phenylcyclohexanecarboxylic acid 3400-45-1, Cyclopentanecarboxylic acid 13064-83-0, trans-4-Methylcyclohexanecarboxylic acid 23635-14-5 38289-27-9, trans-4-Propylcyclohexanecarboxylic acid 38289-28-0, trans-4-Butylcyclohexanecarboxylic acid 38289-29-1, trans-4-Pentylcyclohexanecarboxylic acid 53440-12-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(sequential peptide coupling of, with phenylalanine Me ester and saponification of)

L50 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:85057 HCAPLUS
Correction of: 1987:19047
DN 106:85057
Correction of: 106:19047
ED Entered STN: 21 Mar 1987
TI Preparation of D-phenylalanine derivatives and their use as hypoglycemic agents
IN Toyoshima, Shigeshi; Seto, Yoshiko; Shinkai, Hisashi; Toi, Koji; Kumashiro, Izumi
PA Ajinomoto Co., Inc., Japan
SO Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07C103-84
ICS C07D213-82; C07D307-84; C07C103-737; A61K031-195; A61K031-215
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 196222	A2	19861001	EP 1986-302217	19860326 <--
	EP 196222	A3	19880224		
	EP 196222	B1	19920129		
	R: CH, DE, FR, GB, LI				
	JP 63054321	A2	19880308	JP 1986-61833	19860319 <--
	JP 04015221	B4	19920317		
	US 4816484	A	19890328	US 1988-146719	19880121 <--
	US 34878	E	19950314	US 1993-157564	19931123 <--
PRAI	JP 1985-62276		19850327	<--	
	JP 1986-38111		19860222	<--	
	US 1986-844970		19860327	<--	
	US 1988-146719		19880121	<--	
	US 1989-844970		19890327	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 196222	ICM	C07C103-84
	ICS	C07D213-82; C07D307-84; C07C103-737; A61K031-195; A61K031-215

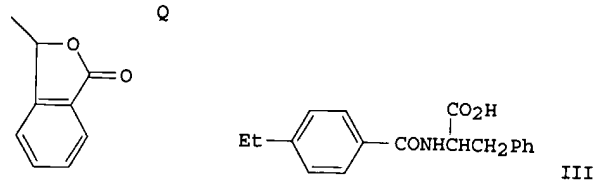
OS CASREACT 106:85057
AB D-Phenylalanine derivs. D-R2CONR3CH(CO2R1)CH2Ph [I; R1 = H, C1-5 alkyl, C6-12 aryl or aralkyl, Q, CH2CO2R3, CHMeOCOR3, CH2OCOCMe3; R2 = (un)substituted C6-12 aryl, 5- or 6-membered heterocyclyl, cycloalkyl, cycloalkenyl; R3 = H, C1-5 alkyl], their salts. and precursors which can be converted thereto in the human or animal body, useful as hypoglycemics, were prepared via conventional N-acylating reactions. D-Phenylalanine in 10% aqueous NaOH was successively treated with Me2CO, 4-EtC6H4COCl in Me2CO, and 10% aqueous NaOH to give 83% acylphenylanine D-II. At 25 mg/kg in mice, D-II decreased blood glucose 34% in min.
ST hypoglycemic D phenylalanine prepn
IT Antidiabetics and Hypoglycemics
(N-acyl-D-phenylalanines)
IT 65-85-0, reactions 98-73-7 98-89-5 496-41-3 824-62-4 943-29-3

4771-80-6 6833-47-2 13064-83-0 16331-45-6 38289-27-9 38289-28-0
65898-38-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-acylation by, of D-phenylalanine)
IT 673-06-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-acylation of)
IT 6066-82-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with cyclopentanecarboxylic acid and cumic acid)
IT 536-66-3 3400-45-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with hydroxysuccinimide)
IT 23635-14-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrogenation of)
IT 10512-92-2 37002-52-1 74204-45-8 85856-40-2 86808-12-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(hypoglycemic activity of)
IT **62067-45-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and N-acylation by, of D-phenylalanine)
IT **7077-05-6P 7084-93-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and esterification of)
IT 51871-58-0P 105746-51-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with D-phenylalanine Me ester)
IT 13828-35-8P 13828-36-9P 105746-50-7P 105746-52-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)
IT 75691-91-7P 105746-24-5P 105746-25-6P 105746-26-7P 105746-27-8P
105746-28-9P 105746-29-0P 105746-30-3P 105746-31-4P 105746-32-5P
105746-33-6P 105746-34-7P 105746-35-8P 105746-36-9P 105746-37-0P
105746-38-1P 105746-39-2P 105746-40-5P 105746-41-6P 105746-42-7P
105746-43-8P 105746-44-9P 105746-45-0P 105746-46-1P 105746-47-2P
105746-48-3P 105746-49-4P **105816-04-4P 105816-05-5P**
105816-06-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as hypoglycemic)
IT 13033-84-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with carboxylic acid succinimidyl esters)

L50 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:19047 HCAPLUS
DN 106:19047
ED Entered STN: 24 Jan 1987
TI Preparation of D-phenylalanine derivatives and their use as hypoglycemic agents
IN Toyoshima, Shigeshi; Seto, Yoshiko; Shinkai, Hisashi; Toi, Koji; Kumashiro, Izumi
PA Ajinomoto Co., Inc., Japan
SO Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07C103-84
ICS C07D213-82; C07D307-84; C07C103-737; A61K031-195; A61K031-215
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 196222 A2		**19861001**	EP 1986-302217	19860326
R: CH, DE, FR, GB, LI				

PRAI JP 1985-62276 19850327
GI



III

AB D-Phenylalanine derivs. D-R2CONR3CH(CO2R1)CH2Ph [I; R1 = H, C1-5 alkyl, C6-12 aryl or aralkyl, Q, CH2CO2R3, CHMeOCOR3, CH2OCOCMe3; R2 = (un)substituted C6-12 aryl, 5- or 6-membered heterocyclyl, cycloalkyl, cycloalkenyl; R3 = H, C1-5 alkyl], their salts, and precursors which can be converted thereto in the human or animal body, useful as hypoglycemics, were prepared via conventional N-acylating reactions. D-Phenylalanine in 10% aqueous NaOH was successively treated with Me2CO, 4-EtC6H4COCl in Me2CO, and 10% aqueous NaOH to give 83% acylphenylanine D-II. At 25 mg/kg in mice, D-II decreased blood glucose 34% in 60 min.

ST hypoglycemic D phenylalanine prepn

IT Antidiabetics and Hypoglycemics
(N-acyl-D-phenylalanines)

IT 6066-82-6, N-Hydroxysuccinimide
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with cyclopentanecarboxylic acid and cumic acid)

IT 536-66-3 3400-45-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with hydroxysuccinimide)

IT 23635-14-5, (S)-(-)-Perillic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrogenation of)

IT 10512-92-2 37002-52-1 74204-45-8 85856-40-2 86808-12-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(hypoglycemic activity of)

IT **7077-05-6P**, trans-4-Isopropylcyclohexanecarboxylic acid
7084-93-7P, cis-4-Isopropylcyclohexanecarboxylic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and esterification of)

IT 51871-58-0P 105746-51-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with D-phenylalanine Me ester)

IT 13828-35-8P, Methyl cis-4-isopropylcyclohexanecarboxylate 13828-36-9P, Methyl trans-4-isopropylcyclohexanecarboxylate 105746-50-7P 105746-52-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)

IT **62067-45-2P**, 4-Isopropylcyclohexanecarboxylic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and N-acylation by, of D-phenylalanine)

IT 75691-91-7P 105746-24-5P 105746-25-6P 105746-26-7P 105746-27-8P
105746-28-9P 105746-29-0P 105746-30-3P 105746-31-4P 105746-32-5P
105746-33-6P 105746-34-7P 105746-35-8P 105746-36-9P 105746-37-0P
105746-38-1P 105746-39-2P 105746-40-5P 105746-41-6P 105746-42-7P
105746-43-8P 105746-44-9P 105746-45-0P 105746-46-1P 105746-47-2P
105746-48-3P 105746-49-4P **105816-04-4P 105816-05-5P**
105816-06-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as hypoglycemic)

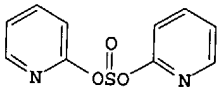
IT 13033-84-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with carboxylic acid succinimidyl esters)

IT 65-85-0, reactions 98-73-7, 4-tert-Butylbenzoic acid 98-89-5 496-41-3 824-62-4 943-29-3 4771-80-6, 3-Cyclohexenecarboxylic acid 6833-47-2, trans-4-Ethylcyclohexanecarboxylic acid 13064-83-0, trans-4-Methylcyclohexanecarboxylic acid 16331-45-6, 4-Ethylbenzoyl chloride 38289-27-9 38289-28-0 65898-38-6, 5-Indanecarboxylic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-acylation by, of D-phenylalanine)

IT 673-06-3
RL: RCT (Reactant); RACT (Reactant or reagent)

(N-acylation of)

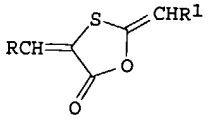
L50 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1986:608739 HCAPLUS
DN 105:208739
ED Entered STN: 13 Dec 1986
TI A new direct esterification method using di-2-pyridyl sulfite as a new coupling agent
AU Kim, Sunggak; Yi, Kyu Yang
CS Dep. Chem., Korea Adv. Inst. Sci. Technol., Seoul, 131, S. Korea
SO Bulletin of the Korean Chemical Society (**1986**), 7(1), 87-8
CODEN: BKCSDE; ISSN: 0253-2964
DT Journal
LA English
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 23
GI



I

AB Dipyridyl sulfite I was used as an efficient coupling agent for the direct esterification of RCO2H(R = Me(CH2)6, PhCH2, Ph2CH, Ph, cyclohexyl, Me3C) under mild conditions.
ST pyridyl sulfite esterification catalyst
IT Esterification
(dipyridyl sulfite and coupling agent for)
IT 1122-58-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(catalyst for esterification reaction)
IT 72762-00-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with **thionyl chloride**, dipyridyl sulfite from)
IT 115-20-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, in the presence of dipyridyl sulfite)
IT 105125-43-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and coupling agent for esterification)
IT 1538-75-6P 5005-35-6P 25774-39-4P 59658-05-8P 89398-02-7P 105147-19-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT 93-89-0P 101-97-3P 106-32-1P 2094-69-1P 3289-28-9P 3469-00-9P 4861-85-2P 5457-66-9P **6553-80-6P** 10276-85-4P 22733-94-4P 37537-23-8P 84443-53-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, by esterification reaction using pyridyl sulfite as coupling agent)

L50 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1986:109513 HCAPLUS
DN 104:109513
ED Entered STN: 05 Apr 1986
TI Syntheses and chemical properties of novel 1,3-oxathiolan-5-one derivatives
AU Ogawa, Kazuo; Yamada, Shozo; Terada, Tadafumi; Yamazaki, Tomio; Honna, Takaji
CS Res. Inst., Taiho Pharm. Co., Ltd., Tokushima, 771-01, Japan
SO Chemical & Pharmaceutical Bulletin (**1985**), 33(6), 2256-65
CODEN: CPBTAL; ISSN: 0009-2363
DT Journal
LA English
CC 28-5 (Heterocyclic Compounds (More Than One Hetero Atom))
OS CASREACT 104:109513
GI



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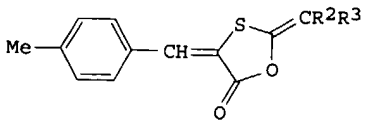
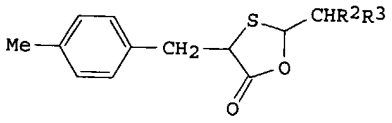


II



III

AB Alkylidenearylidene-1,3-oxathiolan-5-ones I (R = 3-methyl-5-isoxazolyl, Ph, p-tolyl, 4-MeOC6H4, 3,4-methylenedioxyphenyl, ClC6H4; R1 = H, Me, Et) and diarylidene-1,3-oxathiolan-5-ones II (R2 = H, Me; R3 = H, Pr, PhCH2, ClC6H4, PhO, 2-naphthyl, cyclohexylmethyl, CH2CH2CH2CO2Me) were synthesized by treating RCH:C(SH)CO2H with (R1CH2CO)2O or by treating 4-MeC6H4CH:C(CO2H)SCOCHR2R3 with SOCl2 in DMF. Basic hydrolysis and methanolysis of I and II in the presence of LiOH easily occurred to give ring-cleaved products. The catalytic hydrogenation of the two olefinic bonds of II in the presence of 10% Pd/C proceeded without ring cleavage to give 1,3-oxathiolan-5-ones II. The oxidation of I and II with m-chloroperbenzoic acid afforded the corresponding 1,3-oxathiolan-5-one S-oxide derivs.

ST oxathiolanone alkylidene arylidene; mercaptoacrylate cyclization alkanoic anhydride; acylthioacrylate cyclization **thionyl chloride**

IT Cyclocondensation reaction
(of mercaptoacrylic acids with acid anhydrides, alkylideneoxathiolanones from)

IT 93515-29-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(acetylation of)

IT 638-29-9 701-99-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation by, of mercaptotolylacrylic acid)

IT 2550-36-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of di-Et methylmalonate)

IT 609-08-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of, by cyclohexylmethyl bromide)

IT 501-52-0 627-91-8 1878-66-6 51953-02-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(chlorination of)

IT 7282-54-4 93515-28-7 93515-30-1 93515-31-2 93515-32-3 93515-33-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with acid anhydrides, alkylideneoxathiolanones from)

IT 106-31-0 108-24-7 123-62-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with mercaptoacrylic acid, alkylideneoxathiolanones from)

IT 2065-23-8P 100597-71-5P
RL: FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, by methanolysis of oxathiolanone derivative)

IT 536-66-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrogenation of)

IT 645-45-4P 25026-34-0P 35444-44-1P 37859-25-9P 61748-91-2P 100597-38-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation by, of mercaptotolylacrylic acid)

IT **62067-45-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and chlorination of)

IT 100597-37-3P 100597-40-8P 100597-41-9P 100597-42-0P 100597-43-1P 100597-44-2P 100597-45-3P 100597-46-4P 100597-47-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and chlorination-cyclization of, oxathiolanone derivative from)

IT 100597-58-8P 100597-59-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation and hydrolysis of)
IT 100597-64-6P 100597-65-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation and oxidation of)
IT 100597-62-4P 100597-63-5P 100597-68-0P 100597-69-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)
IT 93515-53-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and methanolysis of)
IT 100597-53-3P 100597-54-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and oxidation of)
IT 581-96-4P 93515-27-6P 93515-50-5P 93515-51-6P 93515-54-9P
93515-56-1P 93515-57-2P 93515-58-3P 93515-60-7P 93515-61-8P
93515-62-9P 100597-48-6P 100597-49-7P 100597-50-0P 100597-51-1P
100597-52-2P 100597-55-5P 100597-56-6P 100597-57-7P 100597-60-2P
100597-61-3P 100597-66-8P 100597-67-9P 100597-70-4P 100597-72-6P
100597-73-7P 100597-74-8P 100597-75-9P 100597-76-0P 100597-77-1P
100597-78-2P 100597-79-3P 100597-80-6P 100597-81-7P 100597-82-8P
100597-83-9P 100597-84-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT 100597-39-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate in preparation of methylcyclohexylpropanoic acid)

L50 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1980:41454 HCAPLUS
DN 92:41454
ED Entered STN: 12 May 1984
TI Compositions of cyclohexylcarboxylic acid derivatives
IN Pigerol, Charles; Vernieres, Jean Claude; Eymard, Pierre; Simiand, Jacques; Broll, Madeleine; Lacolle, Jean Yves
PA Labaz S. A., Fr.
SO Belg., 43 pp.
CODEN: BEXXAL
DT Patent
LA French
IC C07C; A61K
CC 24-5 (Alicyclic Compounds)
Section cross-reference(s): 63
FAN.CNT 1

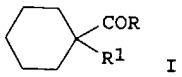
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	BE 875882	A1	19790816	BE 1979-194860	19790426 <--
	CH 641756	A	19840315	CH 1979-3606	19790417 <--
	US 4283420	A	19810811	US 1979-31165	19790418 <--
	DK 7901680	A	19791028	DK 1979-1680	19790424 <--
	DE 2916588	A1	19791108	DE 1979-2916588	19790424 <--
	FR 2432015	A1	19800222	FR 1979-10384	19790424 <--
	FR 2432015	B1	19841116		
	SE 7903687	A	19791028	SE 1979-3687	19790426 <--
	SE 444933	B	19860520		
	SE 444933	C	19860828		
	GB 2023002	A	19791228	GB 1979-14511	19790426 <--
	GB 2023002	B2	19821124		
	GB 2081714	A	19820224	GB 1981-23729	19790426 <--
	GB 2081714	B2	19830323		
	CA 1150150	A1	19830719	CA 1979-326456	19790426 <--
	NL 7903352	A	19791030	NL 1979-3352	19790427 <--
	JP 55004365	A2	19800112	JP 1979-53305	19790427 <--
	JP 60054285	B4	19851129		
	ES 480041	A1	19800716	ES 1979-480041	19790427 <--
	CA 1153777	A2	19830913	CA 1982-409809	19820819 <--
	SE 8304410	A	19830815	SE 1983-4410	19830815 <--
PRAI	GB 1978-16762		19780427 <--		
	CA 1979-326456		19790426 <--		

GB 1979-14511 19790426 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
BE 875882	IC	C07CIC A61K

GI



I

AB Acids and acid derivs. I [R = OH, OM (M = alkali or alkaline earth metal), NH2; R1 = alkyl, alkenyl, alkynyl, alkoxyalkyl, acylalkyl, aryl, arylalkyl, aryloxyalkyl], which exhibited anticonvulsant and sedative activity, were prepared by alkylation, alkenylation, and alkynylation reactions. Thus, cyclohexanecarboxylic acid reacted with allyl chloride, BuLi, and (Me2CH)2NH in THF at room temperature to give I (R = OH, R1 = allyl).

ST cyclohexanecarboxylic acid alkyl prepn sedative; alkylcyclohexanecarboxylic acid prepn anticonvulsant; sedative alkylcyclohexanecarboxylic acid prepn; alkenylcyclohexanecarboxylic acid prepn anticonvulsant; alkynylcyclohexanecarboxylic acid prepn anticonvulsant

IT Anticonvulsants and Antiepileptics
Hypnotics and Sedatives
(cyclohexanecarboxylic acids and derivs.)

IT 4630-82-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(acetylation of)

IT 3289-28-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(addition reaction of, with acetaldehyde)

IT 75-07-0, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(addition reaction of, with cyclohexanecarboxylate esters)

IT 67-64-1, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(addition reaction of, with cyclohexanecarboxylic acid)

IT 107-05-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkenylation of cyclohexanecarboxylic acid by)

IT 98-89-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkenylation, alkynylation and alkylation reactions of)

IT 766-05-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of)

IT 74-96-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of cyclohexanecarbonitrile by)

IT 507-20-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of cyclohexanecarboxylate ester derivative by)

IT 100-44-7, reactions 107-30-2 589-10-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of cyclohexanecarboxylic acid by)

IT 106-96-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkynylation of cyclohexanecarboxylic acid by)

IT 1123-25-7
RL: PROC (Process)
(conversion of, to sodium salt)

IT 55897-67-1 62718-34-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydration of)

IT 41108-87-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and alkylation of)

IT 35618-41-8P 72335-76-3P 72335-82-1P 72335-83-2P 72335-84-3P
72335-85-4P 72335-86-5P 72335-89-8P 72349-73-6P 72349-87-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation of)

IT 72335-66-1P 72335-67-2P 72335-95-6P 72349-75-8P 72349-76-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and anticonvulsant activity of)

IT 1123-24-6P 15826-10-5P 72335-65-0P 72335-68-3P 72335-69-4P
72335-70-7P 72335-71-8P 72335-72-9P 72335-75-2P 72335-77-4P
72335-78-5P 72335-79-6P 72335-80-9P 72335-81-0P 72335-90-1P
72349-72-5P 72349-78-1P 72349-80-5P 72349-81-6P 72349-83-8P
72349-86-1P 72349-88-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and anticonvulsant and sedative activity of)

IT 72335-52-5P 72335-53-6P 72335-62-7P 72349-82-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion of, to acid chloride)

IT 1124-98-7P **1127-07-7P** 27334-43-6P 72335-50-3P 72335-55-8P
72335-58-1P 72335-59-2P 72349-77-0P 72349-79-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion of, to sodium salt)

IT 72335-91-2P 72349-89-4P 72349-94-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and dehydration of)

IT 55897-67-1P 72335-56-9P 72335-57-0P 72348-98-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

IT 72335-96-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with hydrogen chloride)

IT 72335-60-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with phosphorus pentachloride)

IT 72335-97-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with **thionyl chloride**)

IT 72335-61-6P 72335-63-8P 72335-64-9P 72335-93-4P 72349-74-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)

IT 1124-97-6P 41417-87-2P 56164-66-0P 72335-51-4P 72335-54-7P
72335-73-0P 72335-74-1P 72335-87-6P 72335-88-7P 72335-92-3P
72335-94-5P 72349-84-9P 72349-85-0P 72349-90-7P 72349-91-8P
72349-92-9P 72349-93-0P 72349-95-2P 72349-96-3P 72349-97-4P
72349-98-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 2658-60-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hydrogen bromide and acetic anhydride)

L50 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1965:439670 HCAPLUS
DN 63:39670
OREF 63:7166e-h,7167a
ED Entered STN: 22 Apr 2001
TI Interfacial polycondensation of S2Cl2 with polyfunctional alcohols, phenols, amides, and amines
AU Tokarzewski, L.; Szymik, Z.
CS Paedagog Hochsch., Katowice, Pol.
SO Plaste und Kautschuk (**1965**), 12(7), 387-9
CODEN: PLKAAM; ISSN: 0048-4350
DT Journal
LA German
CC 48 (Plastics Technology)
GI For diagram(s), see printed CA Issue.
AB Polysulfide resins are obtained from S2Cl3 and hydroquinone (yield 33.7%), resorcinol (25.57%), phloroglucinol (53.63%), pyrogallol (52.72%), ethylene glycol (18.54%), diethylene glycol (14.90%), triethylene glycol (10.30%), pentaerythritol (59.23%), urea (25.0%), thiourea (49.0%), hexamethylenediamine (54.16%), piperazine (45.94%), m-phenylenediamine (36.20%), benzidine (82.24%), 2,4-diaminoazobenzene (**41.66%**), and 1,8-naphthylenediamine (59.57%). The resins are insol.

powders with a "Thiokol-like" odor. They are resistant to organic solvents, caustic alkalis, and non-oxidizing acids, and have good dielec. properties. The phys., mech., and elec. properties of the resins determined on compression molded samples are: Brinell hardness 9.316.7 kg./mm.2, tensile strength 6.84-43.92 kg./cm.2, impact strength 0.66-2.92 kg.-cm./cm.2, dielec. constant 4.67-26.91, dielec. strength 3->30 kv./mm., dielec. loss factor 0.007-0.05, volume resistivity 7.67 .times. 105 to >2 .times. 1013 ohm-cm., sp. gr. 1.43-1.99 g./cm.3, softening temperature 90-140.degree., heat distortion temperature (Vicat) 70-152.degree., decomposition temperature 120-220.degree., water absorption (14 days) 0.058-6.466%. The supposed structures of these resins deduced from the ir spectra, from the S content, and from the structure of analogous low-mol.-weight compds. are given. The resins from phenols and glycols may have the general formula (OROSS)n, where R is C6H4, CH2CH2, CH2CH2OCH2CH2, or (CH2CH2O)2CH2CH2. The resins from diprimary amines, urea, and thiourea may have the general formula I, where R is (CH2)6, m-C6H4, 1,8-naphthylene, CO, or CS. The resins from piperazine may have the formula II. To prepare the resins, one of the above polyfunctional compds. (0.5 mole) and NaOH were dissolved in 600 ml. H2O, or, if insol., in dilute MeOH (2:1) and cooled. A solution of S2Cl2 in 200 ml. benzene was added in 30-60 min. and the reaction mixture was mixed for 30 min. The amounts of the reactants were stoichiometrical. The temperature of the cooled reaction mixture was 0-10.degree.. The precipitated polysulfide was filtered, purified by boiling with H2O and MeOH, and dried.

IT Dielectric constant, Dielectric dispersion
Dielectric loss
Dielectric strength
Electric properties
Spectra, infrared
(of polysulfides from S2Cl2 and polyfunctional alcs., amides, amines or phenols)

IT Electric resistance
(of polysulfides from S2Cl2 and polysunctional alcs., amides, amines or phenols)

IT Absorption
(of water, by polysulfides from S2Cl2 and polyfunctional alcs., amides, amines or phenols)

IT Sulfides
(poly-, from S2Cl2 and polyfunctional alcs., amides, amines or phenols)

IT 1,8-Naphthalenediamine, polysulfides with S2Cl2
Benzidine, polysulfides with S2Cl2
C.I. Basic Orange 2, polymer with S2Cl2
Diethylene glycol, polysulfides with S2Cl2
Pentaerythritol, polysulfides with S2Cl2
Phloroglucinol, polysulfides with S2Cl2
Piperazine, polysulfides with S2Cl2
Pyrogallol, polysulfides with S2Cl2
Resorcinol, polysulfides with S2Cl2
Triethylene glycol, polysulfides with S2Cl2
m-Phenylenediamine, polysulfides with S2Cl2

IT 1,6-Hexanediamine, polymer with S2Cl2
(amide polymers)

IT 57-13-6, Urea 107-21-1, Ethylene glycol 123-31-9, Hydroquinone
(polysulfides with S2Cl2)

IT 10545-99-0, **Sulfur chloride**, SCl2
(polysulfides with polyfunctional alcs., amides, amines and phenols)

L50 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1939:6498 HCAPLUS
DN 33:6498
OREF 33:986h-i,987a-c
ED Entered STN: 16 Dec 2001
TI Action of **sulfuryl chloride** on pyridine oxide
AU Bobranski, Boguslaw; Kochanska, Lidia; Kowalewska, Anna
SO Ber. (**1938**), 71B, 2385-8
DT Journal
LA Unavailable
CC 10 (Organic Chemistry)
AB Continuation of the work on the action of SO2Cl2 on quinoline oxide (C. **A.** 32, **4166.8**). The HCl salt of pyridine oxide (I) required for the present work was obtained much more conveniently with Bohme's o-HO2CC6H4CO3H (II) (C. A. 31, 3474.7) than by Meisenheimer's method with BzO2H. II is not only more easily prepared and is more stable than BzO2H but has the further advantage of forming the phthalate of I, which is difficultly soluble in ether and seps. from the reaction mixture, free from yellow impurities, after the oxidation. With hot 10% HCl this phthalate gives the HCl salt. Unlike the quinoline analog, I.HCl reacts

with SO2Cl2 neither at room temperature nor after refluxing 4 hrs. When, however, the 2 substances are heated 2 hrs. in a sealed tube at 120.degree., distillation of the excess of SO2Cl2 leaves a yellow oil which, when made alkaline and steam-distilled, yields a water-insol. oil (III) of pyridine-like odor and a small amount of pentachloropyridine, m. 123-4.degree.. Difficulties were encountered in attempts to sep. III into its components with picric acid. The picrate of 4-chloropyridine (IV) immediately precipitated from the alc. solution but could not be thoroughly purified by crystallization; no other product could be isolated. With HgCl2, however, were obtained the double salts of IV and of the 2-Cl isomer (V), the solubilities of which in 100 cc. alc. at 20.degree. are 0.5 and 7.5 g., resp. The relative yields of IV and V are approx. 43:57. The identities of IV and V were established by comparison of the bases and the AuCl3 and HgCl2 compds. with samples prepared by other methods; microphotographs of the crystals of the chloroaurates are reproduced. IV.HgCl2 becomes green at 100.degree., blackens about 230.degree., decomposes 250-60.degree., partially melting; the V compound, V.2HgCl2, m. 177-8.degree., decomposes appreciably in the air and also loses part of its HgCl2 on recrystn. from dilute alc.

IT Mercury chlorides, HgCl2, compound with 2-chloropyridine
Mercury chlorides, HgCl2, compound with 4-chloropyridine
Phthalic acid, compound with pyridine oxide

IT Phthalic monoperacid
(reaction with pyridine)

IT 109-09-1, Pyridine, 2-chloro- 626-61-9, Pyridine, 4-chloro-
(and derivs.)

IT 694-59-7, Pyridine, oxide
(derivs.)

IT 2176-62-7, Pyridine, pentachloro-
(preparation of)

IT 7791-25-5, **Sulfuryl chloride**
(reactions with pyridine oxide)

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